

08-16-04

[Signature]

PTO/SB/21 (02-04)

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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number

09/183,055

Filing Date

November 29, 1998

First Named Inventor

June et al.

Art Unit

1644

Examiner Name

Phillip Gambel

Attorney Docket Number

36119.125US8

Total Number of Pages in This Submission

20

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AUG 19 2004

OFFICE OF PETITIONS

ENCLOSURES (Check all that apply)

- | | | |
|--|---|---|
| <input type="checkbox"/> Fee Transmittal Form | <input type="checkbox"/> Drawing(s) | <input type="checkbox"/> After Allowance communication to Technology Center (TC) |
| <input type="checkbox"/> Fee Attached | <input type="checkbox"/> Licensing-related Papers | <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences |
| <input type="checkbox"/> Amendment/Reply | <input type="checkbox"/> Petition | <input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief) |
| <input type="checkbox"/> After Final | <input type="checkbox"/> Petition to Convert to a Provisional Application | <input type="checkbox"/> Proprietary Information |
| <input type="checkbox"/> Affidavits/declaration(s) | <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address | <input type="checkbox"/> Status Letter |
| <input type="checkbox"/> Extension of Time Request | <input type="checkbox"/> Terminal Disclaimer | <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): |
| <input type="checkbox"/> Express Abandonment Request | <input type="checkbox"/> Request for Refund | |
| <input type="checkbox"/> Information Disclosure Statement | <input type="checkbox"/> CD, Number of CD(s) _____ | |
| <input type="checkbox"/> Certified Copy of Priority Document(s) | Remarks
- Supplemental Petition Under 37 C.F.R. Sec. 1.182 to Withdraw a Recorded Terminal Disclaimer (19 Pages)
- Return Postcard | |
| <input type="checkbox"/> Response to Missing Parts/Incomplete Application | | |
| <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53 | | |

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Colleen Superko, Reg. No. 39,850
Signature	<i>Colleen Superko</i>
Date	August 13, 2004

EXPRESS MAIL LABEL NO. EV 32520170103
DATE OF DEPOSIT 8/13/04

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.



#43

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. 09/183,055 Art Unit: 1644
Applicant: June *et al.* Examiner: Phillip Gambel
Date Filed: November 29, 1998 Conf. No.: 2710
Docket No.: 36119.125US8 Cust. No.: 23483
Title: Method for Selectively Stimulating Proliferation of CD8⁺T Cells

CERTIFICATION UNDER 37 C.F.R. § 1.10

I hereby certify that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office to Addressee" Service under 37 C.F.R. § 1.10 on the date indicated below and is addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

EV 22520169205
Express Mail No.

8/13/04
Date of Deposit

Sharon R. Matthews
Sharon R. Matthews

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION TO CORRECT INVENTORSHIP PURSUANT TO 37 C.F.R. § 1.48(b)

Dear Sir:

Applicants respectfully request that the inventorship of the above-referenced application be corrected by deleting Craig Thompson and Gary Nabel from the list of co-inventors on this application. This amendment to inventorship is required because the inventive subject matter of Craig Thompson and Gary Nabel is no longer being claimed in the instant application.

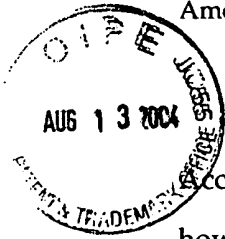
Upon entry of the instant petition to correct inventorship, the co-inventors of the instant application will be: Carl June, Paul Rennert, Gary Gray and Gordon Freeman. Accordingly, the assignees of the instant application will be: The United States as Represented by the Secretary of the Navy, Genetics Institute LLC and Dana-Farber Cancer Institute.

08/17/2004 ANAB11 00000034 080219 09183055
01 FC:1460 130.00 DA

Appl. No. 09/183,055

Our Ref. No.: 36119.125US8

Amendment to Correct Inventorship under 37 C.F.R. § 1.48(b)




Please charge the processing fee set forth in 37 C.F.R. § 1.17(i) of \$130.00 to our Deposit Account No. 08-0219. No additional fees are believed to be due in connection with this filing; however, if any fees are due, the Examiner is requested to charge our Deposit Account No. 08-0219.

If there any questions regarding this matter, the Examiner is invited to telephone the undersigned at the telephone number given below.

Respectfully submitted,

Dated: August 13, 2004


Colleen Superko
Reg. No. 39,850

Correspondence Address:

WILMER CUTLER PICKERING HALE AND DORR LLP

60 State Street

Boston, MA 02109

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Fax: (617) 526-5000



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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE AUG 19 2004

Application No. 09/183,055

Art Unit: 1644

OFFICE OF PETITIONS

Applicant: June *et al.*

Examiner: Phillip Gambel

Date Filed: November 29, 1998

Conf. No.: 2710

Docket No.: 36119.125US8

Cust. No.: 23483

Title: Method for Selectively Stimulating Proliferation of CD8⁺ T Cells

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EU 225201701 05
Express Mail No.

8/13/04
Date of Deposit

Sharon R. Matthews
Sharon R. Matthews

Mail Stop Petitions
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL PETITION UNDER 37 C.F.R. § 1.182 TO WITHDRAW A RECORDED

TERMINAL DISCLAIMER

Dear Sir:

Further to the Petition filed July 29, 2004 to withdraw the Terminal Disclaimer filed on May 13, 2003 in the above-referenced application over U.S. Patent No. 5,858,358 (*see*, Appendix A), Applicants provide the following additional reasons to withdraw the recorded Terminal Disclaimer in the instant application.

Applicants have filed today an Amendment to Correct Inventorship Pursuant to 37 C.F.R. § 1.48(b) in the instant application with the United States Patent and Trademark Office (*see*, Appendix B). Upon entry of the Amendment to Inventorship, the inventorship of the

Instant application will be Carl June, Paul Rennert, Gary Gray and Gordon Freeman.

Accordingly, the assignees of the instant application will be: The United States as Represented by the Secretary of the Navy, Genetics Institute LLC and Dana-Farber Cancer Institute.

The assignees of U.S. Patent No. 5,858,358 are The United States as Represented by the Secretary of the Navy, Genetics Institute LLC, Dana-Farber Cancer Institute and the Regents of the University of Michigan.

Since the ownership of the instant application and U.S. Patent No. 5,858,358 are different, a Terminal Disclaimer in the instant application over U.S. Patent No. 5,858,358 would be improper.

For these reasons as well as those made in the petition filed July 29, 2004, Applicants respectfully request that the Terminal Disclaimer filed in the instant application over U.S. Patent No. 5,858,358 be withdrawn.

No fees are believed to be due in connection with this correspondence; however, if any fees are due, please charge the requisite fees to our Deposit Account No. 08-0219.

The Office of Petitions is invited to telephone the undersigned at the telephone number given below in order to expedite the withdrawal of the Terminal Disclaimer in the instant application over U.S. Patent No. 5,858,358.

Respectfully submitted,

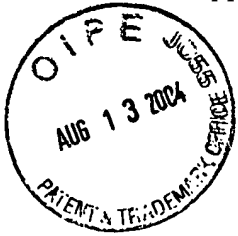
Dated: August 13, 2004


Colleen Superko
Reg. No. 39,850

WILMER CUTLER PICKERING HALE AND DORR LLP
60 State Street
Boston, MA 02109
Tel.: (617) 526-6564
Fax: (617) 526-5000

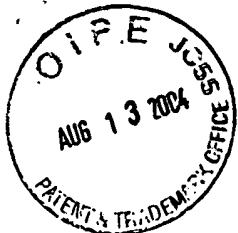
Appl. No. 09/183,055

Suppl. Petition to Withdraw a Recorded Terminal Disclaimer



APPENDIX A

Copy of the Petition filed July 29, 2004 to withdraw the Terminal Disclaimer filed on May 13, 2003 in the above-referenced application over U.S. Patent No. 5,858,358.



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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AUG 19 2004

OFFICE OF PETITIONS

Application No. 09/183,055 Art Unit: 1644
Applicant: June *et al.* Examiner: Phillip Gambel
Date Filed: November 29, 1998 Conf. No.: 2710
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CERTIFICATION UNDER 37 C.F.R. § 1.10

I hereby certify that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office to Addressee" Service under 37 C.F.R. § 1.10 on the date indicated below and is addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

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07/29/2004
Date of Deposit

Marijke Abbès
Marijke Abbès

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION UNDER 37 C.F.R. § 1.182 TO WITHDRAW A RECORDED TERMINAL

DISCLAIMER

Dear Sir:

Applicants respectfully petition to withdraw the Terminal Disclaimer filed on May 13, 2003 in the above-referenced application over U.S. Patent No. 5,858,358.

To recapitulate, in the Final Office Action dated March 6, 2003 (courtesy copy enclosed), the Examiner imposed a rejection under the judicially created doctrine of obviousness-type double patenting in the above-referenced application over U.S. Patent No. 5,858,358 (*see*, Office Action, page 5, section 8). To overcome this rejection, Applicants filed a Terminal Disclaimer over U.S. Patent No. 5,858,358 as part of the Amendment and Response filed on May 13, 2003.

In the subsequent Notice of Allowability dated August 22, 2003, the Examiner indicated in the section entitled "Reasons for Allowance" that the Terminal Disclaimer over U.S. Patent No. 5,858,358 had been recorded by the Patent Office.

Upon careful reconsideration of the currently pending claims of the instant application and those of U.S. Patent No. 5,858,358, Applicants respectfully submit that the Terminal Disclaimer filed in the instant application over U.S. Patent No. 5,858,358 was erroneously filed. Applicants aver that the Terminal Disclaimer was unnecessary because no obviousness-type double patenting exists between the instant application and U.S. Patent No. 5,858,358. Applicants recognize that a provisional obviousness-type double patenting rejection must rely on a comparison of the claims of the two applications in question. Applicants respectfully contend that the claims of U.S. Patent No. 5,858,358 do not render obvious the claims of the instant application.

The claims of U.S. Patent No. 5,858,358 are directed to:

- (1) a method for inducing a population of CD8⁺ T cells to proliferate, comprising activating a population of T cells; and stimulating a CD9 antigen on the surface of the T cells with a ligand which binds the CD9 antigen, the activating and stimulating steps thereby inducing proliferation of the T cells;
- (2) a method for stimulating a population of CD8⁺ T cell to proliferate, comprising contacting a population of T cells with a first agent which stimulates a TCR/CD3 complex-associated signal in the T cells; and a second agent which stimulates a CD9 antigen on the surface of the T cells;
- (3) a method for stimulating a population of CD8⁺ T cells to proliferate, comprising obtaining peripheral blood leukocytes from an individual; isolating a population of CD8⁺ T cells from the peripheral blood leukocytes by negative selection with a combination of antibodies directed to surface markers unique to the cells negatively selected; contacting the population of CD8⁺ T cells with an anti-CD3 antibody immobilized on a solid phase and a ligand which binds a CD9 antigen present on activated T cells, under conditions appropriate for stimulating proliferation of the T cells; separating the anti-CD3 antibody from the T cells and the ligand; monitoring proliferation of the T cells in response to continuing exposure to the ligand by examining cell

size; and restimulating the T cells with the anti-CD3 antibody and the ligand when T cell size has decreased to induce further proliferation of the T cells; and

(4) a method for inducing a population of CD8⁺ T cells to proliferate, comprising activating a population of T cells; and stimulating the population of T cells with a ligand which binds an antigen on the activated T cells, the antigen being recognized by monoclonal antibody ES5.2D8, the activating and stimulating steps thereby inducing proliferation of the T cells.

In contrast, the instant application is directed to a method for stimulating CD8⁺ T cells within a population of T cells to proliferate, comprising contacting a population of T cells with an anti-CD3 antibody, an anti-CD28 antibody, and an anti-CD9 antibody, under conditions appropriate for proliferation of the T cells; separating the anti-CD3 antibody from the T cells and the anti-CD9 and the anti-CD28 antibody; monitoring proliferation of the T cells in response to continuing exposure to the anti-CD9 and the anti-CD28 antibody; and re-stimulating the T cells with an anti-CD3 antibody and the anti-CD9 and the anti-CD28 antibody when the rate of T cell proliferation has decreased to induce further proliferation of the T cells. There is simply no disclosure in the claims of U.S. Patent No. 5,858,358 to stimulate a population of T cells to proliferate using the combination of anti-CD3 antibody, anti-CD9 antibody and anti-CD28 antibody as required by the instant claims. The ordinarily skilled artisan would readily appreciate that the claims of the instant application and U.S. Patent No. 5,858,358 are different, and not obvious over one another.

For the foregoing reasons, Applicants respectfully request that the Terminal Disclaimer filed in the instant application over U.S. Patent No. 5,858,358 to overcome the double patenting rejection be withdrawn.

Please charge the Petition Fee set forth in 37 C.F.R. § 1.17(h) to our Deposit Account No. 08-0219.

Appl. No. 09/183,055

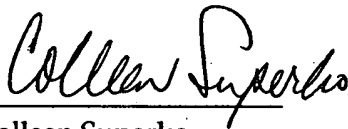
Petition to Withdraw a Recorded Terminal Disclaimer

AUG 13 2004

The Office of Petitions is invited to telephone the undersigned at the telephone number given below in order to expedite the withdrawal of the Terminal Disclaimer in the instant application over U.S. Patent No. 5,858,358.

Respectfully submitted,

Dated: July 29, 2004


Colleen Superko
Reg. No. 39,850

Correspondence Address:

WILMER CUTLER PICKERING HALE AND DORR LLP
60 State Street
Boston, MA 02109
Tel.: (617) 526-6564
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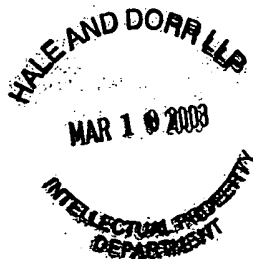
UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/183,055	03/29/1998	CARL H. JUNE	36119-125US8	2710

7590

03/06/2003

Colleen Superko Esq
Hale and Dorr LLP
60 State Street
Boston, MA 02109



EXAMINER

GAMBEL, PHILLIP

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 03/06/2003

28

Please find below and/or attached an Office communication concerning this application or proceeding.

HALE & DORR DOCKETING

RE: 36119-125 US8

Action Date: 6/6/03

Action to be Taken: D10

Docketed By: BMB On: 3/11/03

Office Action Summary

Application No.

09/183055

Applicant(s)

ONE

Examiner

GAMBEL

Art Unit

1644

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address -
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 4/1/02 ; F10/00
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 46, 47, 54-58, 69-71 is/are pending in the application.
- 4a) Of the above claim(s) 1, 46, 47, 54-58, 69-71 is/are withdrawn from consideration.
- 5) ☐ Claim(s) 1, 46, 47, 54-58, 69-71 is/are allowed.
- 6) ☒ Claim(s) 1, 46, 47, 54-58, 69-71 is/are rejected.
- 7) ☐ Claim(s) 1, 46, 47, 54-58, 69-71 is/are objected to.
- 8) ☐ Claim(s) 1, 46, 47, 54-58, 69-71 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on 1/1/02 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on 1/1/02 is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. 09/183055.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☒ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 09/183055
- 4) ☐ Interview Summary (PTO-413) Paper No(s) 09/183055
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. Applicant's submission, filed 7/10/02 (Paper No. 27), has placed this application in compliance with the Sequence Rules.

2. Applicant's amendment, filed 4/1/02 (Paper No. 25), has been entered.

Claims 1, 46-47, 54-58 and 69-72 are pending.

Claims 2-45, 48-53 and 59-68 have been canceled previously.

3. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.

This Office Action will be in response to applicant's arguments, filed 4/1/02 (Paper No. 25).

The rejections of record can be found in the previous Office Action (Paper No. 18).

4. Applicant is reminded to amend the first line of the specification to update the relationship and status of the priority documents.

Applicant's amended priority, filed 4/1/02 (Paper No. 25), does not provide the relationship and status of all of the priority documents for the instant application.

Applicant's amendment to delete the priority to USSN 07/275,433, filed 11/23/88, is acknowledged.

5. This is a rejection under 35 USC § 112, first paragraph, "written description" (and not new matter).

Claims 1, 46, 47 and 56-58 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed for the reasons of record set forth in Paper No. 18.

Applicant's arguments, filed 4/1/02 (Paper No. 25), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 18.

Applicant aver that the invention, as claimed, was conceived at the time of filing of the application.

Applicant aver that the skilled artisan would have known the critical common structural attributes of a ligand for CD9 other than CD9-specific antibodies, namely the ability of the ligand to bind to and stimulate a CD9 molecule on the surface of a CD8⁺ T cell. Further applicant asserts that the skilled artisan would have understood that an anti-CD9 antibody is merely a non-example (non-limiting example) of such a CD9 ligand.

The following of record is reiterated for applicant's convenience.

There is insufficient written description encompassing a "ligand which binds the accessory molecule CD9" because the relevant identifying characteristics such as structure of other physical and/or chemical characteristics of both the "ligand", are not set forth in the specification as filed, commensurate in scope with the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

It does not appear that the specification as filed provides sufficient written description for a ligand other than CD9-specific antibodies that would provide the specificity and activity required by the claimed CD9-specific ligands in the claimed methods.

It does not appear that the specification as filed provides sufficient written description for the critical common structural attributes of a ligand other than CD9-specific antibodies.

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of species or a single species (anti-CD9 antibodies) to support an entire genus. The instant invention encompasses targeting CD9 with any ligand, yet the instant specification does not provide sufficient written description as to the structural features of said ligands and the correlation between the chemical structure and the function of the genus of ligands other than anti-CD9 antibodies. The reliance on the disclosed limited example of anti-CD9 antibodies does not support the written description of any ligand. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological and pharmacological activities. Therefore, structurally unrelated ligands other than anti-CD9 antibodies encompassed by the claimed invention would be expected to have greater differences in their structures, expression and activities.

A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences for identifying a ligand, encompassed by the claimed invention. There is insufficient guidance based on the reliance of anti-CD9 antibodies to direct a person of skill in the art to select or to predict particular sequences as essential for identifying any ligand, encompassed by the claimed invention. Mere idea or function is insufficient for written description; isolation and characterization at a minimum are required.

For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

For example, Li et al. (PNAS 77: 3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

The instant claims do not provide functional characteristics coupled with a known or disclosed correlation between function and structure. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus of ligands, and because the genus is highly variable, anti-CD9 antibodies are insufficient to describe the genus of CD9-specific ligands encompassed by the claimed invention.

The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3).

In the absence of structural characteristics that are shared by members of the genus of ligands and CD9 ligands, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant's arguments are not found persuasive.

6. Claims 1, 46, 47 and 56-58 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "anti-CD9 antibodies" as CD9-specific ligands, does not reasonably provide enablement for any "CD9-specific ligand" to be employed in the claimed methods for the reasons of record set forth in the previous Office Action (Paper No. 18).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments, filed 4/1/02 (Paper No. 25), have been fully considered but are not found convincing essentially for the reasons of record set forth in Paper No. 18.

Applicant argues that the ordinary artisan would have known that the anti-CD9 antibodies described in the specification was a non-limiting example. Applicant asserts that the skilled artisan would have known that any structural characteristics of a CD9-binding ligand, aside from those features necessary to allow binding to CD9, are irrelevant to applicant's invention. Applicant asserts that regardless of its structural characteristics, falls within the claimed invention so long as it actually binds to and stimulates CD9.

The following of record is reiterated for applicant's convenience.

Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies CD9-specific ligands other than those encompassed by "anti-CD9 antibodies" as disclosed in the specification as filed and set forth in claim 69 for example. CD9 ligand may have some notion of the activity of the receptor and ligand, claiming biochemical molecules by a particular name given to the protein (e.g receptor or ligand) by various workers in the field fails to distinctly claim what that protein is and what the compositions are made up of. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any ligand for CD9.

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of species to support an entire genus. The instant invention encompasses any CD9-specific ligand, yet the instant specification does not provide sufficient guidance and direction as to the structural features of said CD9 ligands and the correlation between the chemical structure and the desired CD9 ligand. The reliance on the disclosed limited example of "anti-CD9 antibodies" does not support the enablement for any CD9 ligand.

Applicant is relying upon certain biological activities and the disclosure of a limited representative number of species or a single species of anti-CD9 antibodies to support an entire genus. It has been well known that minor structural differences even among structurally related compounds or compositions can result in substantially different biological and pharmacological properties. Therefore, structurally unrelated ligands encompassed by the claimed invention other than "anti-CD9 antibodies" would be expected to have greater differences in their activities.

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. ligand or receptor) requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence or a limited number of species and in turn utilizing predicted structural determinations to ascertain binding or functional aspects ligands and receptors and finally what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation. In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Because of the lack of sufficient guidance and predictability in determining which structures would lead to CD9 ligands with the desired structural and functional properties and that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of ligand and receptors encompassed by the claimed invention.

Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). In the absence of sufficient guidance and direction to the structural and functional analysis, applicant's reliance upon the CD9-specific antibodies does not appear to provide sufficient enabling support for any ligand or CD9 and so the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

For example, Lederman et al. (Molecular Immunology 28: 1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

For example, Li et al. (PNAS 77: 3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document).

"It is not sufficient to define the recombinant molecule by its principal biological activity, e.g. having protein A activity, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992).

Without sufficient guidance, making and using CD9 ligands would have been unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Applicant's arguments are not found persuasive.

7. Claims 1, 46, 47, and 54-58 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 46, 47 and 54-58 are indefinite in they appear to be incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. For example, the claims lacks the activating and stimulating steps.

Applicant should specifically point out the support for any amendments made to the disclosure.
See MPEP 714.02 and 2163.06

Applicant asserts that the mere addition of an anti-CD3 antibody to a population of T cells will necessarily stimulate the T cells and the CD9 accessory molecule on the T cells is stimulated upon binding by that molecule by a CD9 binding ligand.

Applicant's arguments have been fully considered but are not found convincing for the reasons of record and reiterated herein above.

8. Claims 1, 46, 47, and 54-58 and 69-72 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-33 of U.S. Patent No. 5,858,358 (June et al.) for the reasons of record.

Although the conflicting claims are not identical, the are not patentably distinct from each other because the instant claims, as they read on stimulating the proliferation of T cells, including CD8⁺ T cells, appear to rely upon the same or nearly the same method steps and ingredients, particularly the use of CD3-specific and CD9-specific antibodies

Applicant request that this ground of rejection be held in abeyance until the claims are deemed allowable. Applicant will filed a terminal disclaimer, if a double patenting rejection exists at that time.

9. No claim is allowed.


The instant claims appear to be free of the art, other than the obvious double patenting rejection set forth herein.

10. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.


Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
March 5, 2003

Appl. No. 09/183,055

Suppl. Petition to Withdraw a Recorded Terminal Disclaimer

APPENDIX B

Copy of the Amendment of Inventorship Pursuant to 37 C.F. R. § 1.48(b) filed with the United States Patent and Trademark Office on August 13, 2004.



THE UNITED STATES PATENT AND TRADEMARK OFFICE

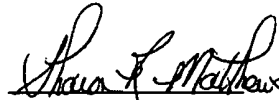
Application No. 09/183,055 Art Unit: 1644
Applicant: June *et al.* Examiner: Phillip Gambel
Date Filed: November 29, 1998 Conf. No.: 2710
Docket No.: 36119.125US8 Cust. No.: 23483
Title: Method for Selectively Stimulating Proliferation of CD8⁺ T Cells

CERTIFICATION UNDER 37 C.F.R. § 1.10

I hereby certify that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office to Addressee" Service under 37 C.F.R. § 1.10 on the date indicated below and is addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

EV 22520169205
Express Mail No.

8/13/04
Date of Deposit


Sharon R. Matthews

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION TO CORRECT INVENTORSHIP PURSUANT TO 37 C.F.R. § 1.48(b)

Dear Sir:

Applicants respectfully request that the inventorship of the above-referenced application be corrected by deleting Craig Thompson and Gary Nabel from the list of co-inventors on this application. This amendment to inventorship is required because the inventive subject matter of Craig Thompson and Gary Nabel is no longer being claimed in the instant application.

Upon entry of the instant petition to correct inventorship, the co-inventors of the instant application will be: Carl June, Paul Rennert, Gary Gray and Gordon Freeman. Accordingly, the assignees of the instant application will be: The United States as Represented by the Secretary of the Navy, Genetics Institute LLC and Dana-Farber Cancer Institute.


Appl. No. 09/183,055
Our Ref. No.: 36119.125US8
Amendment to Correct Inventorship under 37 C.F.R. § 1.48(b)

Please charge the processing fee set forth in 37 C.F.R. § 1.17(i) of \$130.00 to our Deposit Account No. 08-0219. No additional fees are believed to be due in connection with this filing; however, if any fees are due, the Examiner is requested to charge our Deposit Account No. 08-0219.

If there any questions regarding this matter, the Examiner is invited to telephone the undersigned at the telephone number given below.

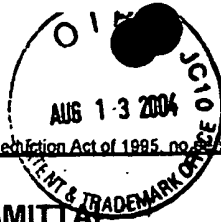
Respectfully submitted,

Dated: August 13, 2004


Colleen Superko
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Approved for use through 07/31/2006. OMB 8551-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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TRANSMITTAL FORM (to be used for all correspondence after initial filing)	Application Number	09/183,055
	Filing Date	November 29, 1998
	First Named Inventor	June et al.
	Art Unit	1644
	Examiner Name	Phillip Gambel
	Attorney Docket Number	36119.125US8
Total Number of Pages in This Submission		3

ENCLOSURES (Check all that apply)		
<input type="checkbox"/> Fee Transmittal Form	<input type="checkbox"/> Drawing(s)	<input type="checkbox"/> After Allowance communication to Technology Center (TC)
<input type="checkbox"/> Fee Attached	<input type="checkbox"/> Licensing-related Papers	<input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences
<input type="checkbox"/> Amendment/Reply	<input type="checkbox"/> Petition	<input type="checkbox"/> Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
<input type="checkbox"/> After Final	<input type="checkbox"/> Petition to Convert to a Provisional Application	<input type="checkbox"/> Proprietary Information
<input type="checkbox"/> Affidavits/declaration(s)	<input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address	<input type="checkbox"/> Status Letter
<input type="checkbox"/> Extension of Time Request	<input type="checkbox"/> Terminal Disclaimer	<input checked="" type="checkbox"/> Other Enclosure(s) (please identify below):
<input type="checkbox"/> Express Abandonment Request	<input type="checkbox"/> Request for Refund	
<input type="checkbox"/> Information Disclosure Statement	<input type="checkbox"/> CD, Number of CD(s) _____	
<input type="checkbox"/> Certified Copy of Priority Document(s)	Remarks - Petition to Correct Inventorship Pursuant to 37 C.F.R. Sec. 1.48(b) (2 Pages) - Return Postcard	
<input type="checkbox"/> Response to Missing Parts/ Incomplete Application		
<input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53		
SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT		
Firm or Individual name	Colleen Superko, Reg. No. 39,850	
Signature	<i>Colleen Superko</i>	
Date	August 13, 2004	

EXPRESS MAIL LABEL NO. EV 22520169205
DATE OF DEPOSIT 8/13/04

This collection of information is required by 37 CFR 1.5. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.